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IS THE OVARIAN CELL PATHOGNOMONIC?

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THE accurate diagnosis of ovarian tumour is of vital importance, as mistakes are by no means rare, even among our most skilful diagnosticians. For example, John Hunter diagnosticated an ovarian tumour, and tapped the woman, who a short time afterwards was delivered of a child showing the marks of the trocar on its shoulder.

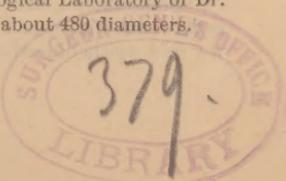
Dr. Washington Atlee mentions a case of pregnancy mistaken for ovarian tumour; the woman was tapped, causing a miscarriage of twins. Mr. Spencer Wells, with his great record in ovariotomy, is obliged to acknowledge twenty-nine mistakes. Of eighty-one cases in which the operation was attempted (*The Principles and Practice of Modern Surgery*, Robert Druitt) no tumour whatever was found in five, and in six others it was not ovarian.

The means of preventing these mistakes are well known, as: Inspection, palpation, percussion, auscultation, the spectroscope, the pulsations of the abdominal aorta (which, according to Dr. Walter F. Atlee,² are pathognomonic), chemical analysis, and the microscope. All methods but the last-named are so well known and tried, that it will not be necessary to discuss them here; it is to the latter, the microscope, that the profession has looked to save it from these embarrassing mistakes. The sac of the tumour presents nothing of a typical or diagnostic value, as the tumour is an epithelial epigenesis of the Graafian vesicle.

But the fluids of the ovarian tumours reveal abundance of cell forms, thought by many to be characteristic. These fluids, under the microscope,

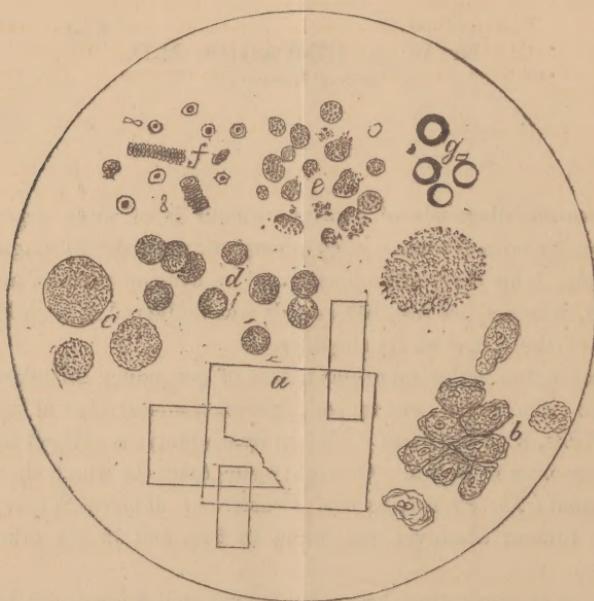
¹ In the preparation of the accompanying paper, I have examined in all about three hundred fluids, both from the American and European hospitals, and from the practice of Dr. Walter F. Atlee, Prof. William Goodell, and the Pathological Laboratory of Dr. Henry F. Formad. The drawing was made under a power of about 480 diameters.

² Amer. Journal Med. Sciences.



often contain oil; blood-globules and plates of cholesterine are frequently seen; epithelial cells, isolated and collected in groups; pus, granular cells, varying in size, which are supposed by some to contain the material upon which the colour of the fluid depends, and a "free, delicate, granular cell" (ovarian cell), which its advocates affirm is characteristic of the ovarian fluid.

The accompanying drawing represents a characteristic ovarian fluid, taken from a patient by Dr. Walter F. Atlee, though it is rarely that I have seen one presenting all the features which are given in the figure.



a. Crystals of cholesterine. b. Epithelial cells. c. Gluge's inflammatory corpuscles. d. Pus-corpuscles. e. Ovarian cell. f. Red blood-corpuscles. g. Oil-globules.

It is (e) the ovarian cell that most concerns us. I regret to differ with Dr. Washington Atlee, Drysdale, and many other authorities, but my investigations with ovarian fluids lead me to conclude that the "free, delicate granular cell" is *not* characteristic of that fluid, as I have seen it in many fluids which were not ovarian, and have examined ovarian fluids in which it was absent.

In connection with these statements the following letters to Dr. Walter F. Atlee speak for themselves: Mallassez, of the College of France, writes that he often examined liquids to determine whether they were ascitic or cystic.

"Sometimes I have been able to affirm the existence of a cyst; but often, I must confess it, have I remained undetermined. When, in the liquid drawn off, we find epithelial cells clearly recognizable (cells caliciform, cells with vibrating

cilia, or simple cylindrical cells), we must admit that these elements proceed from the walls of the cavity that contains the liquid; in other words, that the cavity possesses epithelial lining. This is the case with ovarian cysts. We can thence conclude, that such a liquid is not a peritoneal liquid.

"In fact, in order that epithelial cells be found in a peritoneal liquid there must be communication between the peritoneum, as in some epithelial tumours, which would be revealed by clinical examination.

"When the abdominal liquid does not contain recognizable epithelial cells, but if it contains a notable proportion of granular bodies or crystals of cholesterine, there is still probability that there is an ovarian cyst. Several times I have made myself sure of this. When in the liquid exhibited only some white or red globules exist, the diagnosis appears to me to be very uncertain; such liquids can come just as well from a cyst as from ascites.

"So much for the microscopical examination; now for the chemical analysis. If it is even well established that paralbumen is only met with in ovarian cysts, but never in ascitic fluids, we would have then a very good diagnostic sign. Unhappily I am not able to give you personal information on this point. 20th August, 1878."

Charles Robin writes:—

"It is lost time to hunt with the microscope to distinguish the liquids of cysts of the ovary from the liquids of serous cysts. We must have recourse to chemical analysis. 17th December, 1876."

Dr. Peaslee, in his book (*Ovarian Tumours*, p. 118), says: "I have not been able to detect them [ovarian cell] in the fluid of all cysts known to be ovarian." Dr. Walter F. Atlee thinks, as he expresses it, "that there is no specific cell in ovarian fluids, just as we no longer look for the specific cancer cell in cancerous growths." Spiegelberg and Waldeyer make no mention of them. Mr. Nunn (Brown, *Ovarian Dropsy*, p. 47) does not attach much importance to them as a diagnostic guide. Dr. Braxton Hicks, of Guy's Hospital, and Dr. W. S. Playfair, of King's College Hospital, London, informed me that they placed no reliance whatever on the cell in diagnosis. The so-called "ovarian granular cell" may be described as follows:—

"The cell is usually round, but occasionally oval; it is very delicate, transparent, and contains a number of fine granules, but no nucleus. These granules have a well-defined outline, and glisten like so many particles of diamond dust. The cells themselves differ greatly in size, but the structure is always the same; they are seen as small as $\frac{1}{5000}$ of an inch, and as large as $\frac{1}{2000}$; in some fluids they are much larger, but they generally correspond in size to the pus-cell. The addition of acetic acid causes the granules to become more distinct, while the cell becomes more transparent. When ether is added, the granules become nearly transparent, but the appearance of the cell is not changed. The granular cell (ovarian cell) is distinguished from lymph, white blood-corpuscles, and other cells which it resembles, both by its appearance and its behaviour with acetic acid. The cell wall occasionally has a wrinkled or puckered appearance, and sometimes in the fresh state is seen a body resembling a nucleus; but with acetic acid it merely shows the granules more distinctly, and increases its transparency.

"Gluge's inflammatory corpuscle is larger and more opaque than the ovarian cell, and has the appearance of a collection of oil-globules. Occasionally it has a cell wall; others are wanting in this respect.

"I might add that a cell is sometimes seen in ascitic fluid, depending upon irritation of the peritoneum, which has been mistaken for the ovarian granular cell. In size and somewhat in appearance it resembles the pus-cell, but shows no nuclei on the addition of acetic acid. Their surface is generally granular, but occasionally appears finely wrinkled. It differs from the ovarian granular cell in that it is semi-opaque, and does not present the clearly defined granules of the ovarian cell. It is, as a rule, of a uniform size, $\frac{1}{2000}$ th of an inch in diameter. These cells, however, are not characteristic of the ascitic fluid."¹

Now if the above-described ovarian granular cell were as thoroughly characteristic as its supporters affirm, all doubt in the diagnosis of ovarian dropsy would be forever at rest; but every-day experience does not bear this out; as, for example, a case occurred in the practice of Dr. Walter F. Atlee, on May 7th, 1880, which presented absolutely diagnostic signs of ovarian dropsy, the fluid, upon microscopical examination, showed the most typical ovarian cells in large numbers, the fluid also gave evidence of containing paralbumen, with the well-known test for that substance; these, in conjunction with the other signs of minor importance to us as microscopists, determined the doctor to operate, which he did upon the above-given date. Upon opening the abdominal cavity by the usual method in these cases, *no tumour* whatever was found!

The following is as much of Dr. Atlee's history of the case as concerns our purpose, together with the microscopical report of Dr. Washington Baker, who examined the fluid:—

"Elizabeth Y., æt. 26, measures 47 inches around the waist, a magnificent specimen of health and strength, two months ago began to be unwell; tapped on May 6th, 1880. Fluid coagulable by heat; acetic acid added and boiled, it redissolved, paralbumen. Microscope showed epithelial cells, nuclei in abundance (so-called ovarian granular cell); blood-corpuscles; reaction alkaline."

Dr. Washington Baker's report, May 11th, 1880, states:—

"The fluid is of a greenish-yellow colour, frothing when shaken; deposits a slightly reddish-coloured sediment. Specific gravity 1018. Reaction alkaline; a trace of albumen. Under the microscope are seen epithelial cells, *granular* cells, blood-corpuscles, and granular matter. Coagulable by heat, nitric acid, and alcohol. Paralbumen and fibrinogen. Therefore the fluid under consideration *belongs* to the group of ovarian fluids."

"Upon operating May 7th, 1880, found no cyst, drew away a quantity of fluid, etc., sewed up, etc. etc. June 8th, tapped the patient, removed eleven pints, which, under the microscope, showed nothing but epithelial cells, blood-corpuscles, and granular matter. Specific gravity 1015. Reaction neutral." The woman at the present writing is perfectly healthy, having had no return of her trouble.

I made repeated, careful examinations of the fluid, all of which confirmed the above-given report. The appearance of the cells was such as is seen in the cut on page 429.

¹ Dr. Washington Atlee, Ovarian Tumours.

These ovarian cells acted with reagents precisely as the veritable ovarian cell of Drysdale should act. ("The granular cell found in ovarian fluid, by Thomas Drysdale, M.D.," *Transactions American Med. Assoc.*, 1873.) In fact they were in no way to be distinguished from the cells existing in a case in which the tumour is present, and yet, taken in connection with the presence of paralbumen, etc., how thoroughly did they lead Dr. Atlee astray! Dr. William Goodell has recently had a case of abdominal tumour, the fluid of which, on the first tapping, showed no ovarian cells; on subsequent tappings the cells were seen in sparse numbers, but on operating, the tumour proved to be a typical ovarian cyst. The ovarian cell has been seen in the renal cyst and in the pleural cavity, but I have never had an opportunity of seeing it from those situations.

Dr. Hugh M. Taylor has published an article in the *Virginia Med. Monthly* for 1879, vol. vi. page 209, in which he describes the identity of the cells found in fluid from cystic tumours of the neck, scrotum, etc., with the so-called ovarian corpuscles or Drysdale cell.

I make the statement above that I did not consider the "free granular cell" as characteristic of the ovarian cyst; now the question comes up, what is the ovarian cell, and from whence does it arise, if it is not peculiar to, and owes not its origin to, the ovarian cyst?

In examining many fluids, etc., under the microscope, I have constantly met the pus-cell in various stages of degeneration, or in other words, undergoing the process, as I understand it, which would ultimately turn them out full-fledged ovarian cells. Some of the pus-cells would have one or two glistening granules or fine diamond-like points in them, others quite a number, and still others would be breaking up into the "free delicate granular cell" of Drysdale, and could be distinguished neither by the eye nor by reagents from the veritable ovarian cell of that authority and his followers.

In May, 1880, I examined a fluid in the Laboratory of the University of Pennsylvania, with Dr. Henry F. Formad, for Prof. D. Hayes Agnew, with the following result: "The dark fluid, upon microscopical examination, showed red and white blood-corpuses, pus in stages of degeneration, a very few epithelial cells, and some crystals of triple phosphates." The fluid was drawn from a supposed malignant growth of the rectum, in the male, by a trocar. Some of these pus-cells exhibited but one or two glistening granules, others more, and quite a large majority could be called typical ovarian cells, as it was utterly impossible to distinguish them, either by the eye or reagents, from the ovarian cell found in fluids from the cyst.

If it be true that the ovarian cell is seen in fluids other than ovarian, and also if it be true that it is a degenerated pus-cell, can we not produce this cell artificially? Acting upon this thought, I procured four specimens of healthy, laudable pus: two from amputation stumps, arm and

leg, and two from abscesses. I kept these specimens, each in its own tightly corked bottle, for five weeks, as nearly at the temperature of the body as possible. At the expiration of this time I made microscopical examinations of them with the following result:—

In two I got the typical ovarian cell (amputation specimens), proved so by its appearance and its action with reagents. In the third (abscess of leg) the cell was imperfectly developed, some proving themselves true with reagents, others failing in this respect.

In the fourth and last the cells were not developed at all, either in appearance or reaction with tests; so that the result is: In 1st and 2d specimens, I got typical ovarian cells. In 3d, imperfectly developed. In 4th, entirely absent.

I may add that Dr. H. F. Formad informs me that he has performed the same experiment, using, however, only one specimen of pus, finding it, after the lapse of several weeks, crowded with "ovarian cells."

Let me now recapitulate the points which seem to me to have been proved in this article:—

1. The ovarian cell is not diagnostic of the ovarian tumour.
2. We may have a fluid from an ovarian tumour entirely devoid of the ovarian cell.
3. On the other hand, we may have an abdominal fluid which is not ovarian, presenting the cell in great abundance.
4. With the present state of our knowledge, the accurate microscopical diagnosis of ovarian dropsy is impossible; the most distinguished ovariotomists always make their first incision an exploratory one.

In the examination of the above-mentioned three hundred fluids, I have met the ovarian cell so frequently and have known it to be contained in an ovarian tumour, that, while I do not consider it pathognomonic at all, I still think it merits some weight in making our diagnosis of ovarian cystomata.

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